



# A DRUG UTILIZATION STUDY OF FIXED DOSE COMBINATIONS USED IN HYPERTENSION IN RURAL TERTIARY HEALTH CARE CENTRE OF CENTRAL INDIA

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## ABSTRACT

Hypertension (HTN) accounts for 7.6 million deaths (13–15% of the total) worldwide. The efficacy of antihypertensive agents in lowering blood pressure (BP) and complications of hypertension is well documented. For prime control of BP, two or more antihypertensive agents are required by large number of patients.

**Aims and Objectives:** To analyze the pattern of fixed dose combinations (FDCs) prescribed for treatment of hypertension and blood pressure control in patients who came to Medicine department of a tertiary care hospital of central India, to get a better perspective in the fallacies and implement improvements to overcome them for better management of hypertension.

**Material and Methods:** The present study was a cross-sectional retrospective record based observational study conducted at Medicine Department of NKP Salve Institute of Medical Sciences and Research Centre and Lata Mangeshkar Hospital, Nagpur (M.S.).

**Results:** Out of total 164 case records analyzed, 94 (57.3%) were males and 70 (42.6%) were females. Maximum patients belonged to age group >50 years-64 (39%). FDCs were prescribed in 70 patients out of 164 (42.6%), out of which 2 drug FDCs was used most commonly. Overall most commonly prescribed FDC was that of beta blocker (BB) + calcium channel blocker (CCB) used in 23 patients (32.8%), amongst which metoprolol + amlodipine was most commonly prescribed.

**Conclusion:** In the present study physicians preferred monotherapy over FDCs. Such studies should be conducted on timely basis to detect emerging trends in treatment of hypertension, so that health care policies can be planned accordingly.

**Key Words:** Fixed dose combinations, Antihypertensive agents

## INTRODUCTION

Hypertension (HTN) accounts for 7.6 million deaths (13–15% of the total) and 92 million disability-adjusted life years worldwide, thus acting as major contributor to global burden of disease. It is associated with many deleterious effects like coronary heart disease, stroke, congestive cardiac failure, peripheral arterial disease and renal failure.<sup>[1]</sup> The efficacy of antihypertensive agents in lowering blood pressure (BP) and complications of hypertension is well documented.<sup>[2]</sup> For prime control of BP, two or more antihypertensive agents are required by large number of patients.<sup>[3,4]</sup> Due to multifaceted chemistry between numerous elements like deficiency of apt antihypertensive agents, lifestyle, deri-

sory adherence to drugs/poor patient compliance and meagre acquiescence of physicians with treatment guidelines, majority of patients with HTN do not exhibit fine BP control.<sup>[5,6]</sup> Drug utilization studies have been defined as evaluation of social, medical and economic outcomes of drug therapy.<sup>[7,8]</sup> To achieve lucid and cost-effective health care medical audits are done on a timely basis, out of which analysis of prescribing trends, which examine the current scenario in prescribing practices and thus identify potential fallacies and help in formulating policies to overcome them.<sup>[9]</sup> Such studies also help to identify irrational prescribing habits. Fixed dose combinations (FDCs) are used wherever it is feasible, since they have a positive effect on patient compliance and treatment outcome and this is far more important in view

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of public health care prospective, which has added benefit that specific FDC of drugs in particular ratio is known for known set of population. This results in increased efficacy, cost effectiveness, patient compliance and reduced adverse drug reactions. From physicians point of view also, this is also beneficial since ultimately physician needs drug such that it achieves therapeutic plasma concentration with least adverse drug reaction/s.<sup>[10]</sup> There are very limited available data on use of FDCs used in treatment of hypertension used in India.<sup>[11]</sup> The present drug utilization study analyzes FDCs used in treatment of HTN in order to increase rationality in prescribing medicines and minimize adverse drug reactions. Almost all of the drug utilization studies done on antihypertensive agents are done in urban health care setting, where there is better manpower, health setup, literacy rates, socio-economic status of patients, which is different as compared to rural health care setting, where situation is more or less opposite. Hence the present study was conducted to establish the drug prescribing trend of anti-hypertensive agents used as FDCs in Medicine department of rural health care setting of central India.

### AIMS AND OBJECTIVES

To analyze the pattern of FDCs prescribed for treatment of hypertension in patients who came to Medicine department of a tertiary care hospital of central India, to get a better perspective in the fallacies and implement improvements to overcome them for better management of hypertension.

### MATERIAL AND METHOD

The present study was a cross-sectional retrospective record based observational study conducted at Medicine Department of NKP Salve Institute of Medical Sciences and Research Centre and Lata Mangeshkar Hospital, Nagpur (M.S.). The study duration was of three months from November 2015 to January 2016. Medical case records were obtained from Medical Record Department. The study was initiated after taking approval from Institutional Ethics Committee. Extra care was taken to follow all clauses laid down in protocol at each and every step in the study. Inclusion and exclusion criteria as under:

#### Inclusion criteria:

1. All patients admitted coming to Medicine department who were diagnosed with hypertension.

#### Exclusion criteria:

1. Pediatric patients,
2. Pregnant patients.
3. Hypertensive patients taking drugs other than antihypertensive drugs which can modify blood pressure.

After screening through all inclusion and exclusion criteria total of 164 case records were chosen and included into the study. All demographic details like age, sex, their basal blood pressure (BP), other co-morbidities, fixed dose combinations used was recorded in specially designed information sheet in Microsoft EXCEL 2013. All data was expressed as n (%).

### RESULTS

Out of total 164 case records analyzed, 94 (57.3%) were males and 70 (42.6%) were females. Maximum patients belonged to age group >50 years-64 (39%) followed by 40 (24.4%) in 41-50 age group, 30(18.2%) in 31-40, 25(15.2%) in 21-30 and least in the age group of <20 years age group with 5 (3%) patients (TABLE 1). Mean basal BP was highest in the age group >50 years- 148.8/97.3 mm Hg. It was least in the age group 21-30 years age-134.6/89.5 mm Hg. FDCs were prescribed in 70 patients out of 164 (42.6%). Out of which 2 drug FDCs was used most commonly in 61 patients (87.1%) while 3 drug FDC was used in 9 patients (12.9%). Four drug FDC was not used in any of the patient (TABLE 1). Maximum FDCs were prescribed in the age group 41-50 followed by age group >50 years and least in the age group of <20 years. Sex wise FDCs were used most commonly in males as compared to females (FIGURE 1). Overall most commonly prescribed FDC was that of beta blocker (BB) + calcium channel blocker (CCB) used in 23 patients (32.8%), amongst which metoprolol +amlodipine was most commonly prescribed in 11 patients. Second most commonly prescribed group of FDC was angiotensin receptor blocker (ARB) and diuretic, which was prescribed in 13 (18.6%) patients, followed by angiotensin converting enzyme inhibitor (ACEI) and diuretic FDC used in 11 (15.8%) patients. Losartan + hydrochlorothiazide and ramipril +hydrochlorothiazide was most commonly used in ARB + diuretic group and ACEI + diuretic groups, respectively (TABLE 2, FIGURE 2).

### DISCUSSION

The present study was conducted in Medicine Department of a tertiary care teaching hospital of central India and it included all patients admitted with diagnosis of hypertension. Hypertension being a chronic condition, requires enduring treatment with multiple drugs on a daily basis. FDCs have many proven advantages over use of monotherapy like improved efficacy, reduction in dose of individual drugs, reduced adverse drug reactions and improved patient compliance.<sup>[12,13]</sup> In the present study males were affected more than females with male: female ratio of 1.3. This finding was in contrast to findings of other studies,<sup>[14]</sup> which reported higher incidence in females. This may be due to the fact that present study was done in a rural setup hospital and in rural population women

healthcare is most neglected. Most common age group affected in the present study was in >50 years age group which is in accordance with findings of other study.<sup>[15]</sup> FDCs were most commonly prescribed in age group >50 years and this may be attributed to the fact that old age is associated with numerous co-morbidities and disease advancement. The use of FDCs have an added advantage in such patients since patients in this age group are at risk of age related memory loss and consequently obliviousness. Most common FDC prescribed in the present study was metoprolol+ amlodipine. Metoprolol reduces heart rate owing to its cardio-selective  $\beta_1$  blocker and amlodipine reduces total peripheral resistance due to arterial dilation, and it belongs to dihydropyridine group of CCB. The combination of both complement each other since there is diminution in acutely encountered hemodynamic side effects and fatigue of  $\beta$  blockers when amlodipine is added. Losartan + hydrochlorothiazide was 2<sup>nd</sup> most commonly prescribed.<sup>[16]</sup> Hydrochlorothiazide acts by inhibiting  $\text{Na}^+/\text{Cl}^-$  co-transporter while losartan blocks angiotensin II receptor. It is shown in various studies that the volume reliant status of blood pressure in salt encumbered patients can be changed to a favorable renin reliant status by addition of diuretic, since ACEIs and ARBs are less effective in the former situation.<sup>[17,18]</sup> The Joint National Committee (JNC) guidelines recommend thiazide diuretics to be prescribed alone or as part of combination therapy for most hypertensive patients without compelling indications.<sup>[19]</sup> 3<sup>rd</sup> most commonly prescribed FDC was ramipril + hydrochlorothiazide. As stated above, agents acting through renin angiotensin aldosterone system are complemented by addition of diuretic. Moreover, the side effects of hydrochlorothiazide namely, hypokalemia, hyperglycemia, hypercholesterolemia and hyperuricaemia are reduced by addition of ramipril. Losartan + amlodipine were prescribed in the present study to a significant level. The efficacy of this FDC is well documented as compared to monotherapy, also the probability of development of pedal edema with amlodipine is reduced when it is pooled with losartan.

## CONCLUSION

In the present study physicians preferred monotherapy over FDCs. Beta blocker + calcium channel blocker was most commonly prescribed. Diuretic was most commonly used drug in FDC as is efficacy in combination with many antihypertensive agents is supported by vigorous substantiations. Such studies should be conducted on timely basis to detect emerging trends in treatment of hypertension, so that health care policies can be planned accordingly.

## ETHICAL APPROVAL

Taken prior to the start of the study.

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**Conflicts of Interest:** None declared.

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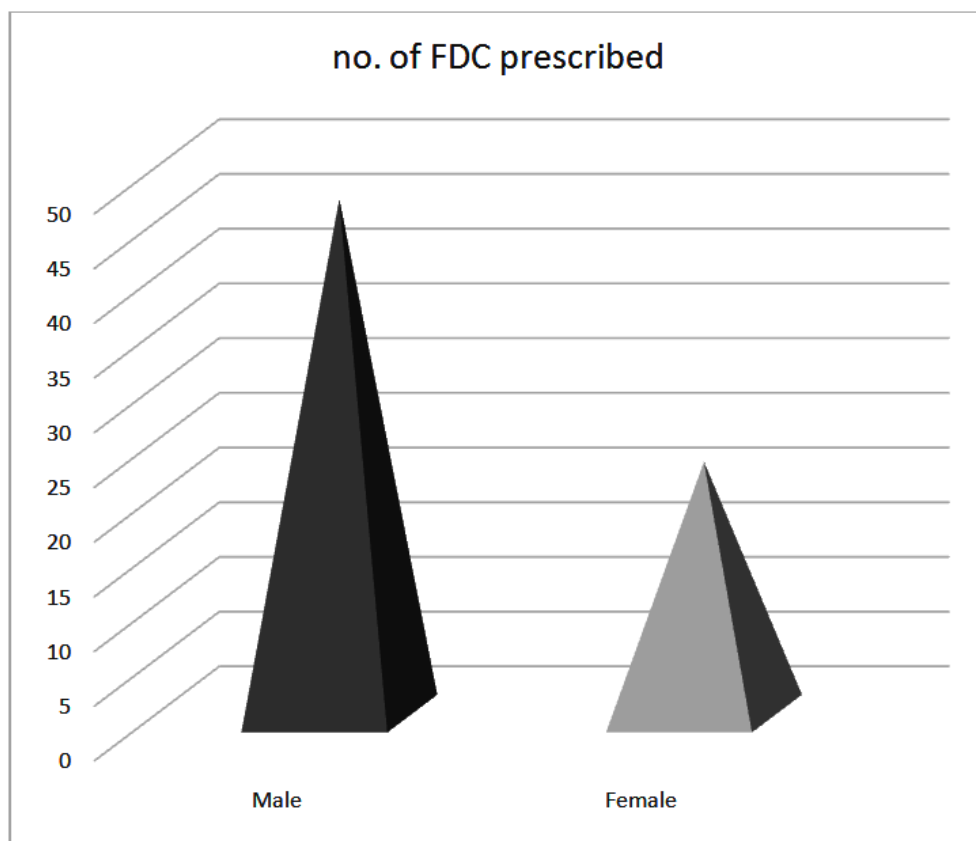
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**Table 1: Showing demographic details and and number of FDCs prescribed.**

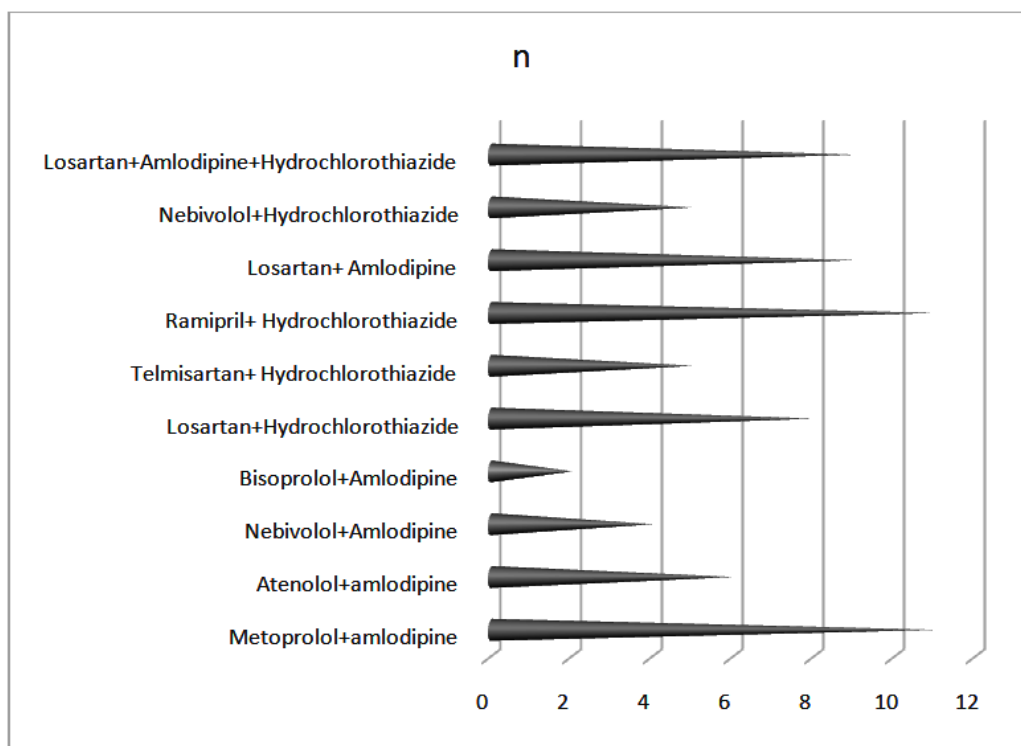
Characteristics	n	%	Total
1. Age:			164
a. >50 years	64	39	
b. 41-50	40	24.4	
c. 31-40	30	18.2	
d. 21-30	25	15.2	
e. <20	5	3	
2. Gender:			
a. Male	94	57.3	164
b. Female	70	42.6	
3. FDC/s prescribed:			
b. double drug FDCs	61	87.1	70
c. triple drug FDCs	9	12.9	
d. quadruple drug FDCs	0	0	

**Table 2: showing specific FDCs prescribed in the present study.**

Classwise FDCs prescribed	Specific drugs used in FDCs	n	Total	%	Max. in age group
1. Beta blocker+CCB	Metoprolol+amlodipine	11	23	32.8	41-50
	Atenolol+amlodipine	6			
	Nebivolol+Amlodipine	4			
	Bisoprolol+Amlodipine	2			
2. ARB+Diuretic	Losartan+Hydrochlorothiazide	8	13	18.6	41-50
	Telmisartan+ Hydrochlorothiazide	5			
3. ACEI+ Diuretic	Ramipril+ Hydrochlorothiazide	11	11	15.8	>50
4. ARB+ CCB	Losartan+ Amlodipine	9	9	12.8	>50
5. Beta blocker + Diuretic	Nebivolol+Hydrochlorothiazide	5	5	7.1	31-40
6. ARB+CCB+Diuretic	Losartan+Amlodipine+Hydrochlorothiazide	9	9	12.8	41-50



**Figure 1:** Showing sex wise FDCs prescribed.



**Figure 2:** Showing number of FDCs prescribed.